

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Pending Claims

Prior to this Amendment, Claims 21-25, 27-31, 33 and 35-40 were pending. By this Amendment, Claims 36, 37 and 40 are cancelled without prejudice. As a result, the pending claims are Claims 21-25, 27-31, 33, 35, 38 and 39.

Introductory Remarks

The Examiner has specified, in paragraphs 2-5 of the Office Action, a series of rejections alleging that the claimed inventions are obvious. These rejections, listed below, are respectfully traversed for the reasons that follow.

None of the prior art cited discloses data showing successful induction of an immune response by a blend of particle populations that differ as to their antigens. Rather, the Examiner's position is to a large extent based on a combination of the references, Shahin et al. and Jones et al. Shahin et al would appear to be far from satisfactory as a reference. Although Shahin et al. obtained successful immunization with intranasal delivery of a blend of populations, they had no data on oral delivery of such blends and indeed no success at all with oral delivery of a single population that comprised a single antigen, FHA. The dramatic difference between the results of

intranasal and oral delivery of a single population illustrate the difficulties in using results with intranasal delivery to predict results with oral delivery. Such a prediction is even more difficult when dealing with the more complex situation of a blend of two antigen populations.

Jones et al. apparently speculate that they are successful with single antigen delivery because they used a different antigen than Shahin did (Jones. p. 492, last par., first 4 lines). If, however, the key to success orally is largely due to the antigen, then Applicant should have had poor results with blends using the same antigen (FHA) that Shahin used. To the contrary, Applicant showed that the use of FHA markedly contributed to improved immunologic efficacy of the other antigen (PTd) in Applicant's blends. Therefore, Applicant has discovered a remarkable benefit to blends that cannot merely be explained by a change in antigen.

The marked enhancing effect of a blend on PTd antigen efficacy can be seen from Figures 6 and 7 of the application, which are discussed in Examples 7 and 8, respectively. In Figure 6, the Log₁₀CFU levels of *B. pertussis* in the lungs is, on the average (days 3, 7, 10, and 14), about 100 times less after oral delivery of FHA-PTd microparticle blends than after oral delivery of PTd microparticles alone. In Figure 7, the Log₁₀CFU levels of *B. pertussis* are shown for FHA-PTd nanoparticle blends. Those levels on days 3, 7, 10 and 14 are on the average comparable to those obtained with microparticle blends in Figure 6.

Applicants results show that the blended populations have surprisingly good efficacy and it is therefore submitted that the claimed inventions are patentable.

Rejection of Claims 21-25 under 35 U.S.C. 103(a) (Paragraph 2 of the Office Action)

The Examiner has rejected the claims over Jones et al (1996) in view of Shahin. Applicants submit that the claims are patentable, Jones and Shahin notwithstanding, for the reasons set forth above under Introductory Remarks above

Rejection of Claims 28-31, 33, and 35-37 under 35 U.S.C. 103(a) (Paragraph 3 of the Office Action)

The Examiner has rejected the claims over Jones et al. (1996) in view of Shahin as applied to Claims 21-25 and further in view of Singh et al. or O'Hagan et al. (U.S. patent 5,603,960).

Claims 36 and 37 have been cancelled. The remaining claims apply to blends of particle populations. The reasons that Jones and Shahin in combination do not make Applicant's invention unpatentable are discussed above under Introductory Remarks above. Singh et al and/or O'Hagan et al do not disclose additional information of a nature that, in combination with Jones and Shahin, would make Applicant's inventions unpatentable.

Rejection of Claim 38 under 35 U.S.C. 103(a) (Paragraph 4 of the Office Action)

The Examiner has rejected the Claim over Jones et al. 1996 in view of Shahin as applied to Claims 21-25, and further in view of Andrianov (U.S. patent 5,807,757). Claim 38 is patentable because it is dependent on Claim 21 which, for the reasons set forth above, is patentable. This does not preclude there being additional reasons for the patentability of Claim 38.

Rejection of Claims 39 and 40 under 35 U.S.C. 103(a) (Paragraph 5 of the Office Action)

The Examiner has rejected the claims as being unpatentable over Jones 1996 in view of Shahin in view of Singh et al or OHagan et al as applied to Claims 28-31, 33 and 35-37, and further in view of Andrianov.

Claim 39 is patentable because it is dependent on Claims 28 which, for the reasons set forth above, is patentable. This does not preclude there being additional reasons for the patentability of Claim 39.

Claim 40 has been cancelled.

In view of the foregoing remarks, it is respectfully submitted that all of the claims now pending in this application are allowable.

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Respectfully submitted,
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CERTIFICATE OF MAILING

I hereby certify that the foregoing Amendment Under 37 CFR 1.116, a Petition for Extension of Time, A Fee Transmittal for FY2002, and a Transmittal Form, re Application Serial No. 09/386,709 are being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope addressed to: Box AF, Commissioner for Patents, Washington, D.C. 20231 on this 17th day of September, 2002.



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